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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/325,189	06/03/1999	MASATAKA KINJO	990360/LH	2516
1933	7590	11/05/2003	EXAMINER	
FRISHAUF, HOLTZ, GOODMAN & CHICK, PC			TUNG, JOYCE	
767 THIRD AVENUE			ART UNIT	
25TH FLOOR			PAPER NUMBER	
NEW YORK, NY 10017-2023			1637	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/325,189	KINJO, MASATAKA	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-39,42 and 43 is/are pending in the application.
- 4a) Of the above claim(s) 9-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7,8,39,42 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Based upon the response filed 8/12/2003, the claims 1-5, 7-39 and 42-43 are pending claims 9-38 are withdrawn from further consideration.

1. Claims 1-5, 7-8, 39 and 42-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Salituro et al. (6,391,544, issued May 21, 2002) in view of Eigen et al. (5,807,677, issued September 15, 1998).

Salituro et al. disclose a method for detecting a target sequence in a test sample employing a pair of primer sequences to generate copies of the target sequence (See column 1, lines 7-10). The first primer and second primer are referred to as a "primer pair" (See column 3, lines 21-23). The first primer is added to the amplification mixture such that its concentration is between 15% to 250% greater than the concentration of the second primer (See column 3, lines 61-64). If desired, a primer can be labeled using methodologies well known in the art (See column 4, lines 12-13). The label can be detectable label, for example fluorophores (See column 5, lines 35-39). The labeled primer was at a concentration of 50 nM and the unlabeled primer concentration was varied at the concentration 25, 37.5, 50 or 62.5 nM. The experiments results are that when the unlabeled primer is present at concentration lower than the labeled primer, higher signals are achieved at higher target concentration and when the concentration of unlabeled primer is higher than or equal to the concentration of labeled primer, the higher signals are achieved at medium target concentration (See column 8, lines 18-40).

Salituro et al. do not disclose evaluating a fluctuation motion of the amplified nucleic acid to quantifying the target nucleic acid and specific ratio the concentration of the primers as claimed in claims 42-43.

Eigen et al. disclose fluorescence correlation spectroscopy (FCS) method, which requires a specific primer sequence, marked with fluorescence dye (See column 2, lines 31-32). The measuring principle with FCS is based on the fact that fluorogenic molecules can be measured in extremely diluted solutions by exposing a small volume element of the solution (See column 2, lines 38-41). The fluorescence correlation spectroscopy (FCS) has a number of advantages compared to the PCR method in which FCS can be used for both single stranded and double stranded nucleic acid molecules and is more direct identifying the individual nucleic acids (See column 3, lines 46-57).

Since the method of Salituro et al. provides the quantitative signal of the labeled amplified nucleic acid products (See column 8, lines 30-40), one of ordinary skill in the art would have motivated to apply the FCS method to the method of Salituro et al. at the time of the instant invention. The motivation is based upon the discussion of the advantage of using FCS as addressed by Eigen et al. above. Moreover, although Salituro et al. do not disclose the specific ratio of the concentration of the primers as claimed in claims 42-43, Salituro et al. do disclose the comparison experiment using different ratio concentration of two different primers. Thus, one of ordinary skill in the art would have optimized the concentration ratio of the two primers based upon the teachings of Salituro et al. It would have been prima facies obvious to carry out the method as claimed.

The response argues that Salituro et al. do not disclose the same asymmetric PCR as in the presently claimed invention in which the response cites the teaching from the disclosure of Salituro et al. that only when the unlabeled primer was present at concentrations over than the labeled primer was a more linear signal produced correlating with target concentration (See

column 10, lines 5-10) and Eigen et al. do not teach or suggest combining FCS with PCR.

However, Salituro et al. discussed how the concentration of the target affects the signal result in terms of the ratio of the unlabeled primer and labeled primer. Claim language does not limit to the concentration of the target nucleic acid. Nevertheless, Salituro et al. do disclose that the labeled primer is in a lower number than the unlabeled primer (See column 8, lines 18-40).

The response further argues that in the present invention, the amount of target nucleic acid contained in a sample before the PCR amplification can be determined based on the number of PCR cycles carried out, until the labeled primer is completely consumed and this is a specific feature of the presently claimed invention. While the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Regarding argument on the teachings of the reference of Eigen et al., it is true that Eigen et al. do not teach or suggest combining FCS with PCR, but Eigen et al. disclose fluorescence correlation spectroscopy (FCS) method which requires a specific primer sequence marked with fluorescence dye (See column 2, lines 31-32). Therefore, based upon the motivation discussed in the Office action mailed 2/26/2003, it would have been prima facies obvious for one of ordinary skill in the art. to modify the method of Salituro et al. by applying the FCS of Eigen et al. to analyze the target nucleic acid.

Applicant's arguments filed 8/12/2003 have been fully considered but they are not persuasive. Thus the rejection is maintained.

2. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Summary

3. No claims are allowable.

Art Unit: 1637


4. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung J.T.
October 23, 2003


ETHAN WHISENANT
PRIMARY EXAMINER